

8EHQ-0504-15566S

05 May 2004



Great Lakes
CHEMICAL CORPORATION

VIA CERTIFIED MAIL
Internal ID #: 04-01



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U.S. Environmental Protection Agency
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Washington, DC 20460

ML 275192

SANITIZED

Attention: TSCA Section 8(e) Coordinator

RE: Submission of Reproductive and Fetal Survival Effects in the Rat via an OECD 422 Guideline Screening Study of Phenol, isopropylated, phosphate (3:1); (CAS No.: 69937-41-7) [

].
(When responding, please refer to JAB-04-013).

Dear Sir:

Great Lakes Chemical Corporation (GLCC) submits this letter of substantial risk notification in accordance with Section 8(e) of the Toxic Substances Control Act, 15 USC 2607(e), and the Environmental Protection Agency's "Statement of Interpretation and Enforcement Policy" thereof 43 FR 1110, 35 seq., March 16, 1978. The notification is in regards to a verbal report and draft Summary Data Tables received from the laboratory that is performing an OECD 422 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test of isopropylated triphenyl phosphate (common name) [

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The test material was administered via oral gavage using corn oil as the carrier vehicle to groups of 12 male and 12 female Sprague-Dawley CrI:CD*(SD)IGS BR strain of rat. The test material was given once daily at dose levels of 25, 100 or 400 mg/kg. Males were dosed for at least 14 days prior to mating and continued to be dosed throughout mating for a minimum of 28 days. Females were dosed for at least 14 days prior to mating, throughout mating and continued to be dosed until one day prior to termination (lactation day 4 for those that delivered, post-mating day 25 or post-cohabitation day 25 for those that did not deliver). A concurrent control group of identical design received the carrier vehicle corn oil on a comparable regimen.

The study design included recording F₀ viability and clinical observations, body weights and food consumption, functional observation battery, locomotor activity, clinical pathology, and parturition and litter observations. F₁ data included litter identification, pup body weights, and appearance and behavior observations. Macroscopic examinations were conducted on all F₀ animals with tissues and organs collected for microscopic examination and relative organ weight determination in accordance with the study protocol. All F₁ pups were examined macroscopically. Tissues and organs were collected for possible microscopic examination only

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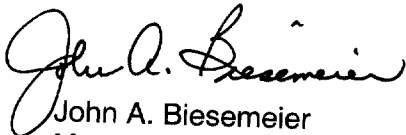
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if deemed necessary by the gross finding. Histopathology of the control and high dose group F₀ animals is currently underway.

Decreased fertility was noted in the high dose group, as 6 of 12 animals with evidence of mating were gravid. The mid-dose group also showed signs of reduced fertility (2 of 11 animals with evidence of mating were gravid and 1 of 12 never conceived). Furthermore, there were effects regarding live litter size and pup survival in the high dose group. Only one of the litters from the 6 litters born in the high dose group survived to lactation day 4. The remaining pups (litters) in this dose group either died or were euthanized *in extremis*.

In addition to the observed reproductive and pups (litters) survival effects, there were effects noted on organ weights in both sexes. The organs affected included absolute and relative weights of the liver, epididymis and adrenal glands of males, and absolute and relative weights of the adrenal glands and relative weights of the ovaries of females. It was the organ weights of the mid and high dose groups that showed the most significant effects. The exception was the increases in female adrenal weights and relative ovary weights, which were observed in a significant dose-related manner for all 3 treated groups.

Sincerely,

A handwritten signature in dark ink, appearing to read "John A. Biesemeier". The signature is fluid and cursive, with the first name "John" being the most prominent part.

John A. Biesemeier
Manager, Regulatory Toxicology
Regulatory Affairs

JAB/jab